REMARKS

Favorable consideration of the claims is respectfully requested. Claims 12-18 were pending. By this Amendment, claims 12-16 and 18 have been amended, claim 17 has been canceled without prejudice or disclaimer, and new claims 19-20 have been added. No new matter has been added. Accordingly, claims 12-16 and 18-20 are pending.

Claims 12-18 were rejected for constituting new matter, thereby not satisfying the written description requirement.

A. The Examiner asserts a new matter rejection based on his view that the specification does not support a viral or nonviral promoter operably linked to p21. Applicants disagree.

The claims as filed in the original specification are part of the disclosure and therefore, if an application as originally filed contains a claim disclosing material not disclosed in the remainder of the specification, the applicant may amend the specification to include the claimed subject matter. In re Benno, 768 F.2d 1340, 226 USPQ 683 (Fed. Cir. 1985). MPEP § 2163.03

Original claim 6 explicitly recites the transfer of p21 cDNA using viral or non-viral vectors. If Examiner believes that persons in the art would not readily appreciate that a viral vector may express cDNAs from a viral promoter a more detailed explanation is respectfully requested.

Similarly, if Examiner believes that expressing cDNAs from a nonviral vector may employ linkage to a non-viral vector, a more detailed explanation is respectfully requested. Thus, the rejection should be withdrawn.

Should Examiner disagree that the rejection be withdrawn because he believes it is imperative to explicitly support the term "operably," he should take into account the standard of written description/new matter requirements. An objective standard for determining compliance with the written description requirement is, "*does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed.*" In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). MPEP § 2163.02.

Persons of ordinary skill would clearly understand that the promoter is *operable* linked to the cDNA, and that the Applicants were in possession of such constructs. To find otherwise would require Examiner to provide an explanation why persons in the art would reasonably believe that an inventor would be claiming an inoperable invention.

In addition, the claims' presumption of patentability implies that an invention must also be presumed operable. In view of knowledge in the art relating to the widespread use of viral and nonviral promoters, persons in the art would readily appreciate that p21 could be expressed from either a viral or nonviral promoter or regulatable or constitutive promoter. Given the state of the art, this would be understood without any reference to these classes of promoters.

Further, the paragraph immediately above the one Examiner referenced, i.e., on page 3, explicitly states that p21 may be transferred in viral or nonviral vectors. Such disclosure would suggest predominantly, that the respective vectors would employ viral or nonviral promoters.

B. Examiner states that there is no support for *providing a second polynucleotide sequence comprising the Adenovirus vector....*

Although Applicants have previously overcome this rejection in the amendment filed on December 4, 2002, in the hope of expediting allowance of the claims, the rejection has been addressed by amendment.

Claims 12 and 13 have been amended to remove the allegedly unsupported terms. Where necessary, the dependent claims have been amended to conform to the amendment to claim 12.

New claims 19 and 20 are specifically drawn to embodiments of the method of claim 12, wherein the DNAs are either linked on the same polynucleotide, or provided as distinct polynucleotides. Support for the embodiment of the method wherein the gene transfer of the relevant polynucleotides is performed with the distinct, physically separate polynucleotides can be found as follows:

1. **Specification, page 3, 2nd paragraph** states that p21 may be transferred as "naked DNA" or as "DNA packaged into vectors which can be of **viral** or **non-viral** nature."
   This sentence expressly discloses an embodiment of the method whereby p21 is expressed in a **non-viral vector**. Accordingly, it is indisputable that expressing p21 in a **non-viral vector precludes p21 DNA from being linked to** the Ad-vector containing polynucleotide to be amplified. In other words, in this embodiment, the p21 and the Adenoviral vector DNA **must** be unlinked.

2. **Original claim 6** specifies that the p21 may be used in viral **OR *non-viral vectors.*** Expressing p21 from a non-viral vector requires that p21 not be linked to Ad-vector DNA. This provides support for the amended claims.

3. **Specification, page 2, text line 5,** reads, "Overexpression of p21 prevents apoptosis of the cells ***after*** infection with the Ad vector to be amplified and improves culture medium conditions."
   Thus, it is clearly disclosed that Applicants contemplate overexpressing p21 ***before*** infecting with the Ad vector DNA. The earlier p21 expression "prepares" the cells to fight off the Adenovirus-induced senescence. This is best accomplished if the p21 and Ad vector DNA are physically unlinked, as covered in new claim 11. When unlinked, the skilled artisan has complete control over determining (and optimizing) the lag period between p21 expression and Ad vector infection.

4. **Original claim 8** describes an embodiment where the p21 is stably introduced into the production cell line. Thus, to carry out the method of producing Adenoviral vectors, the Adenoviral vector DNA **must be transfected at a later time – this can only be performed if the DNAs are physically separate**.
   Person with ordinary skill would understand this because one cannot stably transfect a production cell line with Adenoviral vector DNA because the Adenoviral vector DNA eventually results in lytic infection which kills the cells. No stable transformants could be obtained with the Ad-vector DNA, thus the p21 and Ad-vector DNA must be separated.

5. **Original claim 5** discloses p21 expression from a regulated promoter. It is known in the art that Adenoviral vectors have **no** regulated promoters. Thus, it is clear that the p21 gene was contemplated to be expressed in a context of non-Adenoviral DNA – that is, on a fragment physically separate from the Ad-vector.

In conclusion, the amended and new claims are believed to be adequately supported by the specification, together with knowledge of gene transfer methodology that was available as of the application's filing date.

Allowance is respectfully requested.

CONDITIONAL PETITION FOR EXTENSION OF TIME

If any extension of time for this response is required, Applicants request that this be considered a petition therefore. Please charge the required fee to Deposit Account No. 14-1263.

ADDITIONAL FEES

Please charge any further insufficiency of fees, or credit any excess to Deposit Account No. 14-1263.

Respectfully submitted,
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